



THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MAR 29 2005

Food and Drug Administration
Division of Dockets Management
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Reference: Docket Number 1980N-0208, Proposed Rule and Proposed Order: Bacterial Vaccines and Toxoids

Ladies and Gentlemen:

This comment pertains to section IV of the Proposed Rule and Proposed Order: Anthrax Vaccine Adsorbed – Proposed Order. Anthrax is a major bioterrorism and biowarfare threat against the United States and its armed forces, and the work of the Food and Drug Administration (FDA) to conclude promptly this regulatory process is critically important to public health and national security.

The Department of Defense (DoD) believes the science unequivocally supports the categorization of Anthrax Vaccine Adsorbed (AVA) as Category I (safe, effective, and not misbranded), as proposed by the FDA. The focus of this comment is on one of the issues pertinent to the FDA's administrative review: the work of DoD to evaluate and treat members of the armed forces who report adverse health events that occur after vaccination.

As Assistant Secretary of Defense for Health Affairs, my job is to assist the Secretary of Defense in assuring the nation has available, at all times, a healthy fighting force supported by a combat-ready healthcare system. The Military Health System provides medical care for 9.1 million beneficiaries with a worldwide network of 76 military hospitals, over 500 military health clinics, and the Department's extensive network of private-sector healthcare partners. The Anthrax Vaccine Immunization Program (AVIP) is a critical part of our healthcare system and vaccination with AVA is vital to ensuring a healthy and capable fighting force.

We have heard concerns from a small number of Service members that they experienced serious adverse events after vaccination. We have looked into those concerns vigorously, consulting with nationally and internationally acknowledged experts in multiple disciplines of science and medicine. Our preeminent objective has been to help these Service members as much as we possibly can.

Our physicians, nurses, medics, and allied professionals are trained to relieve suffering wherever they find it. We work hard to arrange appointments for patients according to their personal medical needs with the appropriate medical sub-specialists. We fly patients long distances for specialty visits at military hospitals. For Service members deployed overseas, intercontinental travel for specialty medical care is not uncommon. We use digital photography and telemedicine services to obtain specialty consultation without the need for physical travel. We arrange specialty visits with experts at civilian university hospitals or other centers of excellence closer to where the troops live. Often spouses or medical attendants accompany a Service member for these clinical evaluations. We also arrange conference calls so that spouses, family members, and local physicians are personally involved in the medical evaluation and care-giving process.

We recognize that DoD has more experience than the civilian sector with people vaccinated against anthrax and smallpox. So we consider it our responsibility to share our expertise with private practitioners, state health departments, the Department of Veterans Affairs, and other clinicians and professionals. We do this in person and via journal publications and presentations at professional conferences.

Although there is a risk of adverse events with any vaccine or drug treatment, we endeavor to provide our patients the best possible clinical care. We have commissioned multiple studies and engaged several panels of civilian experts to determine if anthrax vaccination is more harmful than other vaccinations. The FDA is aware of these studies and panels through other communications.

To enhance the quality of healthcare associated with all aspects of immunization, we established Vaccine Healthcare Centers (VHCs), which are centers of clinical excellence, to focus the best of medicine on this aspect of the Military Health System. From October 2003 to September 2004, DoD clinics administered several million vaccinations to Service members. For the same period, our VHCs provided in-depth clinical consultations and/or case-management support to about 600 vaccinated Service members. These 600 Service members received support either on-site at one of the VHCs, or by telephone consultation at their duty station around the globe. When Service members' health conditions affected their ability to perform duties, VHCs assisted with disability evaluations. The Service members had received a variety of vaccinations, most notably smallpox and/or anthrax vaccinations, as well as influenza, tetanus-diphtheria, yellow fever or other vaccinations. They had adverse events after these vaccinations, but not necessarily because of vaccination. The most common diagnoses were headache, joint pain, muscle pain, rashes, and malaise.

Cause-and-effect determinations are often very difficult to make in individual cases. Such evaluations require consideration of many factors, with timing being just one factor. It is a fact of medicine that a cause is never found for many cases of illness.

Nonetheless, our spirit of caring makes us want to alleviate discomfort and enhance quality of life to the maximum extent possible.

The following are examples of vaccine-related healthcare coordinated by the VHCs and allied DoD healthcare providers. A sailor developed a neurologic condition known as Bell's palsy on ship; he was flown off the ship to an onshore hospital for a CT scan and follow-on care. A Service member in Alaska was flown to Washington, DC, for treatment of persistent fatigue and muscle aches; he reports improvement in his symptoms. A reserve-component pilot with recurrent headaches and his wife were flown to a military referral hospital for evaluation, with his flight surgeon participating via conference call. Three merchant mariners were treated at military referral hospitals for evaluation of a muscle-weakness disorder, a cardiac condition, and a skin condition, respectively. For all of these cases, DoD clinicians filed reports to the Vaccine Adverse Events Reporting System (VAERS), so their experiences would be available for future analyses of adverse events after vaccination.

To assess vaccine safety, we use a two-pronged approach. The approach with the greatest scientific power is to use cohort studies to compare anthrax-vaccinated and unvaccinated people. Our efforts in this regard have been reviewed by the Institute of Medicine of the National Academy of Sciences in Chapter 6 of its' Congressionally-chartered 2002 report.

We also use VAERS as a registry of adverse events after vaccination. With our common standards across a globally dispersed health network, the DoD encourages VAERS reporting to a far greater degree than our colleagues in state health departments. We have minimum standards for VAERS reporting above and beyond those required in the private sector. See www.anthrax.mil/media/pdf/ClinicalIssues.pdf and www.vaccines.mil/documents/510armymemo.pdf.

The stories of people who developed health problems after immunization are touching and poignant, whether or not there was any cause and effect relationship. In some cases, their lives have been turned upside down. Their pain and sorrow are all too real. So we redouble our efforts to take good care of them. They deserve nothing less than our best efforts.

When the cases are exceptionally complicated, we ask civilian experts to assist our own experts. DoD took the initiative to have civilian physicians appointed by the Department of Health & Human Services review all 1,857 VAERS reports submitted from March 1998 to February 2002. This panel became known as the Anthrax Vaccine Expert Committee (AVEC). Among the 1,857 reports, 64 involved hospitalization. The AVEC found that 11 of those 64 reports involving hospitalization were certainly or probably caused by anthrax vaccine. All 11 involved allergic or inflammation reactions at the injection site. The AVEC also recommended the anthrax vaccine injection site be

moved from the skin in the triceps area to the deltoid area, to avoid swelling that could pinch the ulnar nerve. Otherwise, this panel detected no patterns of unexpected adverse events related to anthrax vaccination. This level of scrutiny is unprecedented for any US-licensed vaccine.

In 2000, the U.S. Congress asked the National Academy of Sciences to perform a top-to-bottom review of the science underlying anthrax vaccination. Wisely, that civilian panel of experts decided to hear personally from people who believed that anthrax vaccination had harmed them. After weighing all the evidence, the panel concluded that anthrax vaccine causes side effects “comparable to those observed with other vaccines regularly administered to adults.” This report found no evidence that people face an increased risk of serious adverse events immediately after receiving anthrax vaccine, or over the longer term (pages 2, 12, 14).

Further, the IOM panel recommended the AVEC had served its purpose and could be disbanded: “The committee observes that no data that indicate the need for the continuation of special monitoring programs for AVA have emerged, but it recognizes the real concerns of Service members ordered to take the vaccine” (page 202).

For those individuals who’ve developed illnesses following vaccination (even those who we can find no plausible likelihood of cause and effect relationship) we continue working with them to give them the best in clinical medicine. We engage our partners at the Centers for Disease Control and Prevention, Department of Veterans Affairs, civilian universities, and international colleagues, to help our patients. We keep records so that some day we might be able to see patterns in the data that are not apparent to us today.

With all of this in mind, vaccinations still offer the best round-the-clock protection against infectious diseases. Among medications, vaccines are held to the highest standards of safety, because they are mainly given to healthy people to keep them healthy. DoD uses vaccines licensed by FDA to protect our fighting forces.

As a globally dispersed healthcare team committed to quality patient care, we believe excellence in immunization requires:

- Reliable science, published in peer-reviewed medical journals, with active and passive safety surveillance systems that keep our collective eyes and ears wide open.
- Quality care processes in delivering immunizations, with exemptions from immunization granted whenever clinically warranted, using vaccines licensed by the FDA.

- Excellence in clinical care, before and during vaccination and in follow-up for future healthcare needs (at sick call and beyond), regardless of whether or not a vaccine caused a patient's health problem.

With these three principles, we seek to earn the confidence of the troops and their families, with mutual understanding that we owe a duty to care for them, with recognition of their contributions to our nation.

If we can provide you with any additional information about our clinical experience in administering over 5.2 million doses of anthrax vaccine, please feel free to contact Colonel Terry Rauch at (703) 681-1711.

Sincerely,


William Winkenwerder, Jr., MD